Crystallography in the News

August 1, 2019. An experimental vaccine against respiratory syncytial virus (RSV), one of the leading causes of infectious disease deaths in infants, has shown early promise in a Phase 1 human clinical trial. Using protein crystallography, a team of researchers (including The University of Texas at Austin’s Jason McLellan) reported that one dose of their vaccine candidate elicited large increases in RSV-neutralizing antibodies that were sustained for several months.

August 1, 2019. Researchers have identified key sections of a bacterial enzyme MraY that could be targeted with new drugs to inhibit the spread of some bacterial infections. A team of scientists from Hokkaido University in Japan, Duke University in the U.S. and The Catholic University of Korea recently published their findings. Five types of natural products have been discovered to have inhibitory activities against MraY.

August 8, 2019. Mark Schlossman, professor of physics at the University of Illinois at Chicago, has received a $14.1 million, five-year grant from the National Science Foundation to expand the experimental capabilities at NSF’s Chemistry and Materials Center for Advanced Radiation Sources, also known as NSF’s ChemMatCARS.

August 14, 2019. Certain types of toxic algae secrete saxitoxin, one of the world’s most lethal neurotoxins, but freshwater frogs are unaffected as they make proteins that sequester saxitoxin. Recently, a team led by Daniel Minor, at UCSF, used X-ray crystallography to solve the structure of saxiphilin, an antitoxin protein collected from American bullfrogs. They determined how saxiphilin binds with saxitoxin to render it harmless.

August 15, 2019. The National Institutes of Health (NIH) awarded Cornell $17.4 million for MacCHESS (Macromolecular X-ray science at the Cornell High Energy Synchrotron Source), a subfacility of CHESS that attracts hundreds of biomedical researchers each year. As part of its Empire State Development Division of Science, Technology and Innovation (NYSTAR) program to promote jobs in the state, New York state will augment the award with up to $2.5 million over the next five years.

August 15, 2019. Using X-ray crystallography, researchers in Japan and the U.K. have uncovered an unusual protein activity in rice that can be exploited to give crops an edge in the evolutionary arms race against rice blast disease, a major threat to rice production around the world. Magnaporthe oryzae, the fungus that leads to rice blast disease, creates lesions on rice plants that reduce the yield and quality of grain.

August 16, 2019. Mario Wriedt, Associate Professor of Chemistry & Biomolecular Science and CAMP Distinguished Professor at Clarkson University, recently offered an intensive 4-day Single Crystal X-ray Diffraction (SCXRD) workshop, Problems, Errors & Pitfalls in Single Crystal Structure Analysis, at Clarkson University’s Main Campus, Potsdam NY, in early August. Rigaku is proud to have been a cosponsor of this workshop.

Product Spotlight

HyPix-Arc 150°: Curved photon counting X-ray detector

Rigaku HyPix-Arc 150° is a unique, curved Hybrid Photon Counting (HPC) X-ray detector for single crystal diffraction applications. HyPix-Arc 150° has the highest 26 range at a single position available for the home lab.

Collect more data in a single exposure with less reflection profile distortion.

The HyPix-Arc 150° offers 150 degrees angular coverage from edge to edge. This is more than enough to collect complete single crystal diffraction data, according to IUCr guidelines, for even Cu Kα X-ray wavelength from a single theta position. High and low angle data are measured at the same time, under the same conditions for better scaling, faster data and reduced dose time. A curved detector minimizes peak distortion by ensuring that, even at short crystal-to-detector distances, diffracted beams are closer to...
We are pleased to announce that we will be holding a two day user meeting and discussion group at the Rigaku Europe HQ in Neu Isenburg near Frankfurt Airport. The meeting will start at 10am on Thursday 26th September running until the afternoon of Friday 27th September. This year's meeting will be jointly held between the single-crystal and powder diffraction groups. Please join us to discover the latest developments at Rigaku in single crystal and powder X-ray diffraction and to chat about your research, experiences, and issues.

Attendance Form

**Wizard TIME: Membrane protein extraction detergent screening kit.**

Membrane protein require detergent solubilization for purification and crystallization. The Wizard TIME screen consists of 84 different formulations. Its utility in identifying those detergent reagents that successfully extract a membrane protein from a membrane preparation. Each detergent formulation consists of a detergent at 2% (w/v) concentration, the stabilizing co-detergent cholesterol hemisuccinate and a buffer.

Features:
- Lowest reflection profile distortion
- Faster data collection
- Higher 2θ coverage in a single image
- All reflections measured under the same conditions
- Capture more diffracted photons per exposure

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**Lab in the Spotlight**

**Department of Chemistry at Emory University**

In June of 2017, the first XtaLAB Synergy-S in the Western Hemisphere was installed at the Department of Chemistry at Emory University. In just over two years the instrument, at the guidance of John Bacsa, has produced over 1000 structures. The XtaLAB Synergy-S was purchased through an award from the National Science Federation. The XtaLAB Synergy-S includes copper and molybdenum PhotonJet sources equipped with Osmic optics, and the proven Rigaku HyPix-6000HE Hybrid Photon Counting (HPC) detector. The advanced high-brilliance sources and a HPC detector with its small pixel size and zero background noise assist in collecting data from the very small crystals, poorly crystalline materials, biological materials and even protein crystals that make up the more than one thousand successful structures.

Dr. John Bacsa
Facilities Director
Crystallography Lab, Emory University
email: jbacsa[at]emory.edu

Synergy-S at Emory has produced over 1000 structures! John is on the far right.

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**Useful Link**

CCTBX team are conducting a survey to find out which parts of the CCTBX are the most interesting for users with the intention of providing or enhancing the documentation for the most popular libraries. If you found yourself in the predicament of wanting to use the CCTBX but decided to stay away from it because the documentation was non-existent or obscure, please let them know by filling out the questionnaire (we are told it's anonymous).
CrysAlisPro V40 has been released on the Rigaku Oxford Diffraction Forum.

The major features of version 40 include:

- 15% off, expires 11/29/19. Code: TIME
- Automated/manual version updating platforms
- Support of all new Synergy and ROD
- Significantly faster processing in dc profit (the 64 bit version, up to 32 cores)
- Extended support for multi-core use (in Ewald3D live in the 64 bit version)
- Updated StructureExplorer
- Support of new AutoChem4.0 with 32 and 64 bit versions

For more information, visit the Rigaku Reagents website.

www.Rigakuxrayforum.com

Selected Recent Crystallographic Papers

New discovery in crystallography: correlation of terahertz time-domain spectra with crystal structures and photoluminescence properties of mononuclear/binuclear diimine–Cu(i)-phosphine complexes. Zhu, Ning; Wang, Guo; Lin, Sen; Li, Zhong-Feng; Xin, Xiu-Lan; Yang, Yu-Ping; Liu, Min; Jin, Qiong-Hua. CystEngComm. 8/7/2019, Vol. 21 Issue 29, p4275-4288. 14p. DOI: 10.1039/c9ce00729f.


A novel structurally characterized haloacid dehalogenase superfamily phosphatase from Thermococcus thioreducens with diverse substrate specificity. Havlickova, Petra; Brinsa, Vitezslav; Brynda, Jiri; Pachl, Petr; Prudnikova, Tatyana; Mesters, Jeroen R.; Kascakova, Barbora; Kuty, Michal; Pusey, Marc L.; Ng, Joseph D.; Rezacova, Pavlina; Kuta Smatanova, Ivana. Acta Crystallographica: Section D, Structural Biology. Aug2019, Vol. 75 Issue 8, p743-752. 10p. DOI: 10.1107/S1600576719009986.


Highly oxygenated meroterpenoids from the Antarctic fungus Aspergillus terreus. Feng, Wenyu; Chen, Chunmei; Mo, Shuyuan; Qi, Changxing; Gong, Jiaojiao; Li, Xiao-Nian; Zhou, Qun; Zhou, Yuan; Li, Dongyan; Lai, Yongji; Zhu, Hucheng; Wang, Jianping; Zhang, Yonghui. Phytochemistry. Aug2019, Vol. 164, p184-191. 8p. DOI: 10.1016/j.phytochem.2019.05.015.


Functional Relevance of Interleukin-1 Receptor Inter-domain Flexibility for Cytokine Binding and Signaling. Ge, Jiwan; Remesh, Soumya G.; Hammel, Michal; Pan, Si; Mahan, Andrew D.; Wang, Shuying; Wang, Xinquan. *Structure*. Aug 2019, Vol. 27 Issue 8, p1296-1296. 1p. DOI: 10.1016/j.str.2019.05.011.

**Book Review**

*Bottle of Lies: The Inside Story of the Generic Drug Boom*  
By Katherine Eban  

Katherine Eban’s *Bottle of Lies* is a remarkable piece of investigative journalism, one she has been working on for over a decade, though the story she tells has roots digging even decades deeper. The focus of her narrative is the Indian pharmaceutical company Ranbaxy Laboratories. Founded by the Singh brothers in 1961, Ranbaxy was operated by the family for the majority of its years of operation. Despite being worth billions of dollars, the
14. Janet Smith and Hao Wu quickly organized a Virginia Pett and Richard Bromund recorded and edited the session, which includes presentations from Jack Johnson, Eddie Arnold, Hao, Rui Zhao and S. Saif Hassan. The ACA has posted the video for all to enjoy.

**Videos of the Month**

Michael Rossmann was scheduled to give the opening keynote at the ACA Annual Meeting this past July. As you know Michael passed on May 14. Janet Smith and Hao Wu quickly organized a celebration of life in lieu of the keynote lecture. Virginia Pett and Richard Bromund recorded and edited the session, which includes presentations from Jack Johnson, Eddie Arnold, Hao, Rui Zhao and S. Saif Hassan. The ACA has posted the video for all to enjoy.

**Watch the Video**

**Subscribe to Rigaku eNewsletters**

Each month, Rigaku distributes two eNewsletters: *The Bridge*, which focuses on Materials Analysis, and *Crystallography Times*, which concentrates on X-ray crystallography. 


Sings ran Ranbaxy like the family-owned-and-operated corporation it was. The company essentially folded in 2014 when it was absorbed by Sun Pharma in the wake of enormous controversy, including recalls and reports of glass fragments in prescription capsules.

But, as Eban herself admits in her opening Author’s Note, her interest in generic prescription drugs did not start with Ranbaxy. In 2008, the host of an NPR radio show called *The People’s Pharmacy* reached out to Eban with concerns expressed by his listeners that their generic drug replacements for brand-name pharmaceuticals were not working. Patients with an established brand-name drug regimen found themselves relapsing when their prescriptions switched to the cheaper, more affordable generic version.

Eban did what investigative reporters do best--she investigated. Her first piece on generic drugs was published in *Self* in 2009. It was her reporting for that first article that inspired *Bottle of Lies*.

Ranbaxy was the focus of an investigative follow-up piece Eban wrote for *Fortune* in 2013. It was in May of that year that the corporation’s corrupt manufacturing and management practices became the center of media attention. Felony charges were brought against the company in the United States as the result of more than half a decade of FDA investigations, sparked by the actions of a single whistleblower: Dinesh Thakur. The company pleaded guilty, to the tune of a $500 million dollar settlement.

Ranbaxy’s fall from grace--it went from winning awards for brand trust to publicly pleading guilty to multiple felony drug fraud counts--consumes the majority of Eban’s narrative. Her key protagonist, Dinesh Thakur, is the former employee turned whistleblower who brought evidence of the company’s malpractice to the FDA. Thakur’s journey, from a respected employee at Bristol Meyers-Squibb, one of America’s prestige brand-name pharmaceutical companies, to one who resigned amidst a cloud of controversy at a generic drug company in India, provides a lens through which Eban encourages her readers to view the web of lies and deceit that dominate the generic drug industry.

The Ranbaxy news is already over half a decade old at this point. There is some semblance of justice as one reads, knowing the bad guys got caught, so to speak. Reading *Bottle of Lies* is like watching *The Untouchables*--you know Elliot Ness got Al Capone in the end, because Capone died in jail. But you still watch the movie because you want to know how--and that's why you need to read *Bottle of Lies*.

Though Thakur dominates much of the narrative, other crusaders of pharmaceutical justice make noteworthy and repeated appearances, such as FDA inspector Peter Baker. Baker uncovered the unsettling reality that generic drug companies not only manufacture and distribute defective drugs to American consumers, they do so around the world. Often, the generics shipped to third-world countries in Africa are those that did not pass muster to be sent to the United States. We may not be getting the good stuff, but Americans are also not the ones getting the worst stuff.

At the heart of the generic drug controversy is the very definition upon which they are based: bioequivalence. As long as a generic drug has the same amount of active ingredient (give or take) as the name-brand drug for which it is being substituted, it is considered an equal substitution. But there is a lot more to prescription medication than active ingredients, and not all generics are created equal. At the end of the day, do generics cost less money to purchase at the pharmacy than name-brand prescriptions? Oftentimes, insurance covers the full cost of the generic, rendering it seemingly free to the average consumer. But the real cost of generic prescription medication is often that of patient health.

If you have ever taken a generic prescription medication, you need to read this book, especially if you take a generic prescription medication on a regular basis.

*Disclosure: Katherine Eban spoke to a class I attended as a journalism student at NYU about her reporting on Ranbaxy, and the process by which she conducted her investigative reporting.

Review by Jeanette S. Ferrara, MA